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EXAMINER	
SINGH, ANOOP KUMAR	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 11/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/811,136	RAPP ET AL.	
	Examiner	Art Unit	
	Anoop Singh	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-65* is/are pending in the application.

4a) Of the above claim(s) *56-65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/17/05, 9/21/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments to the specification filed on June 28, 2004 has been received and entered.

Election/Restrictions

Applicant's election without traverse of claims 1-55 (group I) in the reply filed on August 23, 2006 is acknowledged.

Claims 56-65 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on August 23, 2006.

Claims 1-55 are under consideration.

Drawings

The drawing/figures are objected to because tables and sequence listings included in the specification must not be duplicated in the drawing. See C.F.R. 1.58(a) and § 1.83. Applicants are advised that upon issuance of a patent, the complete text of the sequence listing submitted in compliance with 37 C.F.R § 1.821-1.825 will be published as part of the patent. Applicants should amend the specification to delete any

figures which consist only of nucleic acid or protein sequence which have been submitted in their entirety in computer readable format (as SEQ ID Nos) (see figures 9-19). In this case, no further detail to the sequence is supplied in the figure and is effectively the SEQ ID number.

Claim Objections

Claims 27 and 55 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the instant case, claims merely recite the inherent property of method recited in independent claims 1 and 28. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing transgenic chicken by directly injecting NLB-attP retroviral vector comprising DNA which includes a nuclear

localization peptide (SEQ ID NO: 13) and polyethyleneimine (PEI) into germinal disk of stage X embryo to obtain exogenous protein expression in serum, sperm and egg white of transgenic chicken, does not reasonably provide enablement for making any transgenic avian or using any cell or stage of embryo or using any other vector as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In determining whether Applicant's claims are enabled, it must be found that one of skill in the art at the time of invention by applicant would not have had to perform "undue experimentation" to make and/or use the invention claimed. Such a determination is not a simple factual consideration, but is a conclusion reached by weighing at least eight factors as set forth in In re Wands, 858 F.2d at 737, 8 USPQ 1400, 2d at 1404. Such factors are: (1) The breadth of the claims; (2) The nature of the invention; (3) The state of the art; (4) The level of one of ordinary skill in the art; (5) The level of predictability in the art; (6) The amount of direction and guidance provided by Applicant; (7) The existence of working examples; and (8) The quantity of experimentation needed to make and/or use the invention.

The office has analyzed the specification in direct accordance to the factors outlines in *In re Wands*. MPEP 2164.04 states: "[W]hile the analysis and conclusion of a lack of enablement are based on factors discussed in MPEP 2164.01(a) and the evidence as whole, it is not necessary to discuss each factor in written enablement rejection." These factors will be analyzed, in turn, to demonstrate that one of ordinary

skill in the art would have had to perform "undue experimentation" to make and/or use the invention and therefore, applicant's claims are not enabled.

The claims are directed to methods of producing a transgenic avian by introducing into an avian cell a nucleic acid comprising a transgene, an integrase activity and a cationic polymer and then introducing the avian cell into a recipient avian wherein the recipient avian produces an offspring which includes the transgene. Subsequent claims limit the avian to include chicken while avian cells to include avian stage X avian embryo. The claims are further directed to transgenic avian and an egg produced by the transgenic avian.

The present invention provides a method of producing transgenic avians, such as chickens, comprising a recombinant nucleic acid molecule that expresses a heterologous gene in one or more cells in the animal. It is noted that specification also contemplates transfer of a transfected nucleus to an enucleated recipient cell that may then develop into a zygote and subsequently an adult bird (see page 48, lines 24 bridging to page 49). The specification asserts that transgenic bird could be produced by introducing into embryonic cells the nucleic acid construct comprising an attB recombination site capable of recombining with a pseudo-attP recombination site located within the nuclear genome of the organism such that nucleic acid fragment of interest is stably integrated into the nuclear genome of germ line cells of a mature bird (see page 49, lines 14-24). While the specification has contemplated that methods of the invention may be used to create any transgenic avian, the guidance provided by the specification correlated only to stage I cytoplasmic injection using DNA injection directly

into the germinal disk and injection of NLB-attP retroviral injection into stage X chicken embryo resulting in transgenic chicken. In addition, the specification while providing guidance for using bacterial artificial chromosome containing human monoclonal antibody in the egg white at a concentration of 350 ng/ml or 12 ug per egg. It is unpredictable if the transgenic avian, particularly a chicken, could produce adequate amounts of exogenous protein that is to be harvested for pharmaceutical or industrial use as contemplated by the specification and claims using the methods disclosed in the instant application. Given the lack of guidance provided by the specification it would have required undue experimentation for one of skill in the art to make and use the invention as claimed without a reasonable expectation of success.

As a first issue, the claims embrace the creation of transgenic avian, particularly a chickens. The specification has contemplated that transgenic avian could be used to produce exogenous proteins, particularly cytokines such as interferon in their eggs, wherein the exogenous proteins are collected for pharmaceutical or industrial uses (see page 50). The specification has asserted that such animals could be created by cytoplasmic injection of a nucleic acid molecule encoding a gene of interest directly into the germinal disk or transfection of stage X embryo. The specification has provided a working example correlating only to transfection of the stage X embryo in chicken with NLB vector or cytoplasmic injection with integrase activity and BAC containing chicken ovomucoid gene with cDNA for a human monoclonal antibody with an attB sequence to produce monoclonal antibody in the egg white at a concentration of 350ng/ml. While the specification purported that an ~12 ug would be produced in the chicken eggs, the

specification failed to quantify the amount of human antibody actually produced in the other avian eggs (see example 10; page 64). The specification also purported that a genus of protein encoded by the gene of interest could be produced in a transgenic chicken in large yields (but such appeared to be a prophetic teaching as the chickens were not made (see the specification on page 50, lines 11-25). It would be unpredictable if chicken (or the avian embraced by the claims) could be used as a method to produce antibody if they produced exogenous protein in small quantities such as 350 ng/ml. See Ivarie R (Trends in Biotechnology, 2003 21(1): 14-19), which observed that exogenous protein produced by transgenic chickens in the range of 38μg/ml was far below those required for commercialization. See the section bridging pages 15-16. As such, the specification does not appear to provide guidance correlating the exemplified chicken to produce protein or antibody or any other protein, in enough quantity particularly in light of the observations of Ivarie. Finally, the specification has not provided guidance with respect to levels of exogenous protein expression or duration of expression of exogenous protein. Moreover, it is apparent from the lack of guidance provided by the specification, would require further experimentation to practice the instantly claimed method so that a relevant amount of exogenous protein is produced and secreted into egg white, blood or any other tissue for any cytokine or human antibody as contemplated in the claims 11-18 and 38-45. Therefore, it is unpredictable if the methods would result in any transgenic avian that would produce any desired protein in amount sufficient as contemplated in this application.

As a second issue, independent claims 1 and 28 are directed to a method of producing any transgenic avian by introducing into any avian cell a nucleic acid comprising any integrase activity and any cationic polymer and then introducing that avian cell into any recipient avian wherein the recipient avian produces an offspring which includes transgene. It is noted that instantly claimed invention embrace every possible cell type as embryo as source wherein the embryo is developed *in vitro* or *in vivo*, however, the specification does not provide any specific guidance as to how the method would be carried out using any avian cells. Given the broadest reasonable interpretation, as recited these cells would also encompass introducing a nucleic acid comprising a transgene, an integrase activity and a cationic polymer in any cell including somatic cell and using any other method such as transferring the nucleus of the cell into any enucleated recipient cell and transferring recipient cell into a recipient avian that produces an offspring. The state of art summarized by the references of Wolf et al (Journal of Biotechnology 65: 99-110, 1998); Stice et al (Therigeneology, 1998, 49: 129-138); Yanagimach et al (Molecular and Cellular Endocrinology, 2002, 187, 241-248); Oback and Wells (Cloning and Stem Cells, 2002, 4, 169-174) and Kuhholzer and Prather (The Society for Experimental Biology and Medicine, 2000, 224: 240-245,) disclose limitation of routine method of nuclear transfer. For instance, Wolf et al emphasize several factors that influence embryo cloning by NT, such as the state of development and cell cycle of the donor cells, the choice of recipient cell, the method of activation of oocyte (see entire article). The specification does not provide any guidance to these parameters. Stice et al reported timing of embryonic genome activation might

be partly responsible for species-specific differences. Stice et al further noted that method used for cloning sheep where the donor cell was in G0 could not be used in other animal species (see the last paragraph on page 131). This clearly suggests that method used in one animal or species could not be used in another animal or species, the specification does not provide any guidance how claimed method would be practiced in any avian cell. Yanagimachi et al state that "perhaps no single protocol for cloning that works for all species, because, the characteristics of an oocyte and donor cells are from species to species. A protocol that is best for a given species may not be suitable for another species. Technical details must be worked out for each species". It is emphasized that applicants have provided no guidance in this regard. In summary, the specification as filed is not enabling for the claimed invention because the state of the art of producing transgenic avian from any cell into any recipient cell and transfer of nucleic acid in a cell that develops into embryo in a recipient avian was not predictable and an artisan would have required extensive experimentation to practice the claimed invention and such experimentation would have been undue since the experimentation was not routine, and the state of the art was unpredictable and the specification did not teach how to address the limitation and unpredictable nature of the invention.

As a third issue, claims 1-55 embrace a method that is directed for producing transgenic avian by introducing any cells that may include embryonic cells such as isolated avian blastodermal cells (see page 40, lines 14-17). The art at the time of filing further held that transgenic technology using embryonic cells was not predictable for any species other than mouse (Hochepied et al Stem Cells, 2004, 22: 441-447; pp 444,

right column, lines 1-3). Since the specification contemplates using embryonic cells to produce transgenic avians, ES cells from various species are required to produce various species of avians The state of the art is such that blastodermal technology is to produce transgenic avian was unpredictable and evolving at the time of filing of this application. Ivarie (Trends in Biotechnology, 2003, 14-19) cites Pain who describes long term culture of non-transfected, blastodermal cell that provided germline transmission, however, no transgenic birds have been made using transfected ES cell or PGCs. The biggest obstacle to overcome in making transgenic birds using transfected ES cell or PGCs is the loss of germline competence during culture of transfected ES cells and PGCs (see page 14, column 2, paragraph 3 and page 17, column 1, paragraph 2 and last two sentences bridging to columns 1-2 page 17 column 2, last sentence). Therefore, at the time of filing of this application, transgenic avians could not be accomplished using ES or blastodermal cells. The specification fails to provide sufficient guidance to make transgenic avians by teaching obtaining blastodermal cells. In absence of any specific guidance an artisan would have to perform undue experimentation to make and use the invention to produce transgenic avian using blastodermal cells.

As a fourth issue, the claims broadly embraced creation of all transgenic avian subsequently limiting to chicken. The specification contemplated that avians such as chicken, turkey, duck, goose, quail, pheasants, parrots, finches, hawks, crows and ratites including ostrich, emu and cassowary are embraced by the invention (see specification on page 14, lines 13-15). The specification has provided guidance

correlating to creation of transgenic chicken by cytoplasmic injection of a nucleic acid molecule encoding a gene of interest directly into the germinal disk or transfection of stage X embryo. As discussed above, the transgenic chicken could not produce relevant amounts of monoclonal antibody for collection. The guidance provided by the specification does not extrapolate to all other avians embraced by the claims. Particularly, an extrapolation cannot be made to other avians in light of the biological diversity embraced by the claims. There is no evidence of record correlating the biological processes of egg production between species that would enable one of skill in the art to extrapolate the working example of chicken to all the other species embraced by the claims to produce enough quantity of protein. In addition, to the general lack of guidance with respect to use of other species embraced by the claims, the other species embraced by the claims are subject to all of the issues discussed above. Given the lack of guidance provided by the specification it would have required undue experimentation for one of skill in art to make and use the invention as claimed without a reasonable expectation of success.

As a fifth issue, independent claims 1 and 28 recite introducing into avian cell a nucleic acid comprising a transgene, an integrase activity and a cationic polymer. The specification teaches that a plasmid encoding for the integrase protein is transfected into the target cells. The specification also teaches that the early avian embryo transcriptionally silent until it reaches about 22,000 cells and injection of the integrase mRNA or protein is expected to result in better rates of transgenesis (see paragraph 295 of the published application). As recited integrase activity can be introduced in any

cell of any stage of development by any means. However, it is unclear whether instant claims contemplate introducing nucleic acid or nucleic acid encoding enzyme or a protein. Since, it is generally known in the art and specification also discloses that avian embryo is transcriptionally silent until it reaches about 22,000 cells (supra), it is not apparent how an artisan would be able to practice the methods steps using any stage of avian embryo as broadly recited in the instantly claimed invention resulting in expression of plurality of gene encoding cytokine or other protein.

As a final issue, the claims 1-18, 22-23, 25-45, 50-55 also embrace administration of any cell comprising a transgene an integrase activity and a cationic polymer that is introduced in to any recipient avian, wherein the recipient avian produces an offspring which includes the transgene. The specification contemplated that perhaps delivery of a stage X embryo to an ovary or oviduct of an avian resulting in creation of a transgenic avian that transmits a transgene through the germline of the avian. However, the specification has failed to provide guidance-correlating administration of a stage X embryo to ovary with introducing any other avian cell introduced at any site in avian that resulted in creation of transgenic avian. For example, it is not apparent how any transgenic avian could be produced since instant claims do not necessarily require introducing avian cell to ovary. It is noted that specification teaches that embryo comprising the transgene could be surgically transferred to recipient hen via ovum transfer method as described in the specification (see paragraph 60 of the specification). It is not apparent how any avian cell comprising transgene introduced into recipient avian at any site would produce an offspring that would

produce an transgenic avian. Furthermore, even if avians embryos are in fact targeted with a transgene, it is not apparent how introducing avian embryo at any site would result in an offspring. It is not apparent how introducing chicken embryo comprising transgene surgically transferred to recipient hen via ovum transfer method could be extrapolated to administration introducing any other avian cell comprising transgene introduced at any site of a recipient avian, particularly in light of all the species embraced by the claims resulting in germ line transmission. It is emphasized that neither prior art nor specification provided any specific guidance in using any avian cell rather prior art show unpredictability associated with use of any other cells or use of nuclear transfer methods as discussed before (supra). Given the lack of guidance provided by the specification it would have required undue experimentation for one of skill in art to make and use the invention as claimed without a reasonable expectation of success.

In conclusion, in view of breadth of the claims and absence of a strong showing by applicant, in the way of specific guidance and direction, and/or working examples demonstrating the same, such invention as claimed by applicant is not enabled for the claimed inventions. The specification and prior art do not teach method of transgenic avian by introducing an avian cell comprising nucleic acid and introducing any avian cell into any recipient avian to produce protein in egg, serum or any other tissue. An artisan of skill would have to perform undue experimentation to practice the method as claimed because the art of transgenic avian for producing antibody was unpredictable at the time of filing of this application as supported by the observations in the art record.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 28 are vague and indefinite to the extent that they recite a limitation nucleic acid comprising an integrase activity. It is unclear whether nucleic acid has integrase activity or it encodes an enzyme that has an integrase activity. The meets and bounds of this limitation cannot be determined. Claims 2-27 depend on claim 1, while 29-55 depends on claim 28. Appropriate correction is required.

Claims 7 and 34 recites the limitation "signal" in claim. There is insufficient antecedent basis for structural relationship of "signal" to the rest of the product "introduced". Appropriate correction is required.

Claims 8 and 35 are vague and indefinite because it is not clear how the nucleotide is associated with a nuclear localization signal during its introduction into the cell. It is unclear how NLS is associated with nucleic acid comprising transgene. Appropriate correction is required.

Claims 12 and 39 are vague and indefinite to an extent they recite a limitation coding sequence is expressed "in the blood". It is not clear whether coding sequence is expressed in the blood of in a cell of the blood. Appropriate correction is required.

Claims 13 and 40 are vague and indefinite to an extent they recite a limitation coding sequence is expressed "in the sperm". Since sperm is usually transcriptionally inactive. It is not clear whether coding sequence is expressed in the sperm or may be only present in sperm. Appropriate correction is required.

Claims 13 and 40 are vague and indefinite to an extent that these claims require the expression of coding sequence in the sperm of the transgenic avian; however, as recited not all transgenic avian would be male offspring hence meets and bounds of the claim cannot be determined. Appropriate correction is required.

The term "increased efficiency of transgenic avian relative .." in claims 27 and 55 are relative term which renders the claim indefinite. The term "increased efficiency" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2, 11-12, 14-29 and 34-35, 38-55 are rejected under 35 U.S.C. 102(e) as being anticipated by Sutrave et al (US patent application no 2003/0061629, effective filing date 09/21/2001).

Sutrave et al teach methods for producing a transgenic avian by isolating primordial germ cells (PGCs) from the blastoderm of a stage X avian embryo and then modifying the isolated PGCs, such that the cells incorporate at least one transgene and then transferring the modified PGCs into blastoderm of an avian embryo, hatching the embryo; and testing for the presence of the transgene or expression of the protein encoded by the transgene (see abstract). It is noted that the method of Sutrave also contemplates using retroviral vector that inherently would have integrase activity for introducing transgene in the cell (see page 11, paragraph 113). Furthermore, Sutrave et al also disclose that Cre and loxP transgenes could be inserted into the chicken genome via mediated transgenesis either simultaneously or separately resulting in stable integration into the chicken genome (see page 10, paragraph 101-102). Sutrave et al teach introduction of the vector to the cell may be aided by first mixing the nucleic acid with polylysine. In addition, Sutrave teaches using a transfecting agent for enhancing the uptake of heterologous DNA segment into an avian cell including poly (ethylenimine) (PEI) (see page 5, paragraph 52). It is note that the method could

produce polypeptide including cytokine, erythropoietin, a hormone, an immunoglobulin or more specifically interferon (see paragraph 26). Although, Sutrave et al do not explicitly teach a nuclear localization signal, however, Sutrave et al contemplated signal sequences for optimal expression (see paragraph 56) and also disclosed that vector may be provided with 3' UTR that may be of SV40 late region (see paragraph 110). Since the breadth of independent claims, 1 and 28 requires introducing a nucleic acid comprising a nuclear localization signal. The teaching of Sutrave et al would meet the claim limitation of SV 40 comprising NLS in the vector contemplated by Sutrave et al to transfect avian cells. The exemplified transgenic chicken shows the presence of the transgene in the blood and egg white as determined by PCR and western blot (see example 3). Claims 25-26 and 53-54 are directed to a transgenic avian and eggs produced by a transgenic avians. These claims are product by process claims. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. Given, the steps of the method used to produce the animal, the transgenic avian and eggs are merely required to comprise a nucleic acid comprising a transgene and integrase activity in the cells. Sutrave et al also taught an avian egg which contains protein exogenous to the avian species and allows the expression of exogenous proteins (supra). The transgenic avian and egg disclosed by Sutrave and those embraced by the instant claims appear to be structurally same. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially

identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977).

Thus, the teachings of Sutrave et al anticipate all of the instant claim limitations.

Claims 26 and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Mansoor et al (Immunotechnology, 1998, 4: 115-125)

The claims are directed to eggs produced by a transgenic avians. The claims are product by process claims. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Since the transgenic avian was created by introducing into an avian cell a nucleic acid comprising a transgene and then introducing the avian cell into a recipient avian, the resulting egg will not necessarily comprise the transgene. Moreover, claims 26 and 54 do not specify a particular protein, polypeptide or peptide. Therefore, any teaching of a bird egg anticipates the claim.

Mansoor et al taught chicken eggs comprising human immuno globulins. See the abstract.

Thus, the teachings of Mansoor et al anticipated instant claim limitation.

Claims 25 and 53 are rejected under 35 U.S.C. 102(b) as being anticipated by Sherman et al (Nature Biotechnology, 1998, 16: 1050-1053, IDS).

The claims are product by process claims directed to a transgenic animal, particularly a bird that comprises a transposon-based vector in lumen of its oviduct. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Given, the steps of the method used to produce the animal, the animal is merely required to comprise a nucleic acid comprising a transgene and integrase activity in the cells. It is emphasized that cationic polymer is not given any patentable weight in the claimed transgenic avian since it is only required for enhanced delivery of the transgene

Sherman et al taught creation of germline transgenic chickens using a mariner transposon-based vector. See the abstract. Since the chickens transmitted the mariner vector through the germline every cell, including cells of the ovary and oviduct, in the offspring would comprise the vector that would have integrase activity.

Thus, the teachings of Sherman anticipated all of the instant claim limitations.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sutrave et al (US patent application no 2003/0061629, effective filing date 09/21/2001), Calos (US 6,632672, dated 10/14/2003, IDS) or Kuhn et al (WO 02/38613, dated 5/16/2002; IDS).

Sutrave et al teach methods for producing a transgenic avian by isolating primordial germ cells (PGCs) from the blastoderm of a stage X avian embryo and then modifying the isolated PGCs, such that the cells incorporate at least one transgene and then transferring the modified PGCs into blastoderm of an avian embryo, hatching the embryo; and testing for the presence of the transgene or expression of the protein encoded by the transgene (see abstract). It is noted that the method of Sutrave also contemplates using retroviral vector for the stable integration of transgene in the cells (see page 11, paragraph 113). Furthermore, Sutrave et al also disclose that Cre and

loxP transgenes that could also be inserted into the chicken genome via mediated transgenesis either simultaneously or separately resulting in stable integration into the chicken genome (see page 10, paragraph 101-102). Sutrave et al teach introduction of the vector to the cell may be aided by first mixing the nucleic acid with polylysine. In addition, Sutrave teaches using a transfecting agent for enhancing the uptake of heterologous DNA segment into an avian cell including poly (ethylenimine) (PEI) (see page 5, paragraph 52). It is note that the method could produce polypeptide including cytokine, erythropoietin, a hormone, an immunoglobulin or more specifically interferon (see paragraph 26). Although, Sutrave et al do not explicitly teach a nuclear localization signal, however, Sutrave et al contemplated signal sequences for optimal expression (see paragraph 56) and also disclosed that vector may be provided with 3' UTR that may be of SV40 late region (see paragraph 110). Since the breadth of independent claims, 1 and 28 requires introducing a nucleic acid comprising a nuclear localization signal. The teaching of Sutrave et al would meet the claim limitation of SV 40 comprising NLS in the vector contemplated by Sutrave et al to transfect avian cells. The exemplified transgenic chicken shows the presence of the transgene in the blood and egg white as determined by PCR and western blot (see example 3). Claims 25-26 and 53-54 are directed to a transgenic avian and eggs produced by a transgenic avians. These claims are product by process claims. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. Given, the steps of the method used to produce the animal, the transgenic

avian and eggs are merely required to comprise a nucleic acid comprising a transgene and integrase activity in the cells. Sutrave et al also taught an avian egg which contains protein exogenous to the avian species and allows the expression of exogenous proteins (supra). The transgenic avian and egg disclosed by Sutrave and those embraced by the instant claims appear to be structurally same. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). However, Sutrave do not explicitly teach a phiC31 integrase for site directed integration of the transgene.

Calos et al teach a method of site-specifically integrating a polynucleotide sequence of interest in the genome of a eukaryotic cell (see abstract). Calos described many recombinases that could be used in the method including the site-specific recombinases that are encoded by a phage including phiC31 (see column 3, lines 22-25). Calos et al teach that the recombinase may be introduced into the cell concurrently with targeting construct. It is noted that Calos et al contemplate that site-specific recombinase is introduced into the cell as a polypeptide (see column 4, lines 1-2) or alternatively it is introduced into the cell as a polynucleotide encoding the recombinase and an expression cassette. Calos teaches construct for site-specific integration of a polynucleotide sequence into the genome of a eukaryotic cell comprising a vector, a polynucleotide of interest operably linked to a eukaryotic promoter, and a first recombination site, wherein the genome of the cell comprises a second recombination

site native to the genome and recombination between the first and second recombination sites is facilitated by a site-specific recombinase (see column 2, lines 51-65 and column 4, lines 3-17). Calos also contemplates transgenic animals including chicken in all stages of development including embryonic and fetal stages whose genomes have been modified by using the method and composition to obtain site-specific integration of the nucleotide (see column 24, lines 64-67 bridging to column 25, lines 1-6). Calos described methods of producing transgenic nonhuman animal including introducing into a single cell embryo a nucleic acid construct, comprising recombination site capable of recombining with an recombination site found within the genome of the organism from which the cell is derived and a nucleic acid of interest, in a manner such that the nucleic acid of interest is stably integrated into the DNA of germ line cells of the animal (see column 25, lines 23 bridging to column 26). The method disclosed by Calos for creating permanent genomic modification is to employs a strategy so that DNA becomes part of the existing chromosomes. It is noted that Calos describes that only retroviruses provide efficient integration but has several limitation that could be overcome by using the method of Calos (see column 57-66). Although Calos generally embraced the idea to deliver nucleic acid construct by cationic lipid in a subject for the therapeutic purpose (see column 28, lines 15-18) but he did not explicitly teach a method of producing transgenic avian by also introducing into avian cell a cationic polymer along with construct disclosed by Calos.

Kuhn et al teach a method that provides highly efficient modification of genome of mammalian cell by site specific recombination containing a fusion protein that

comprises phiC31 recombinase and a peptide sequence which directs the nuclear uptake of the fusion protein (see abstract). It is noted that Kuhn et al contemplates making transgenic nonhuman organism (see page 8, line 21) using a DNA encoding the recombinase and nuclear localization sequence (NLS) (see page 8). Kuhn did not limit the method to any specific organism, but he generally embraced the idea of using nucleic acid encoding fusion protein for stable integration of transgene in the genome of different organisms. Kuhn et al did not teach a method to produce transgenic chicken.

Accordingly, in view of the teachings of Sutrave, it would have been obvious for one of ordinary skill in the art, at the time the claimed invention was made, to modify the method of producing transgenic chicken taught by Sutrave to include phiC31 or nucleic acid encoding fusion protein taught by Kuhn et al /Calos for making transgenic avian with a reasonable expectation of success. One of ordinary skill in the art would have been sufficiently motivated to make such a modification, as Calos had described benefits of using alternative methods such as phiC31 or cre based recombinase for stable integration of transgene as compared to retroviral vector in producing transgenic nonhuman animal including chicken (supra). In addition, Calos/Kuhn sought to create transgenic nonhuman animal including chicken using recombinase based method for stable integration of transgene in the genome. Therefore, given that phiC31 based recombinase and NLS were available for use to integrate gene of interest in chicken as per the teachings of Calso/Kuhn, it would have obvious for an artisan to use the method of Sutrave to use phiC31 based recombinase with or without NLS to create transgenic chicken to produce human protein as disclosed in the instant application.

One who would practiced the invention would have had reasonable expectation of success because Sutrave had already described the method to produce transgenic chicken to produces interferon or any other protein. Calos/Kuhn had already described use of other recombinase and NLS that could have been used in conjunction with the construct for making transgenic chicken to express gene of interest. Thus, it would have only required routine experimentation to modify the method disclosed by Sutrave to include nucleic acid comprising integrase activity with NLS and transgene to make transgenic chicken to produce human protein as required by instant invention.

Claims 9-10 and 36-37 have been included in the rejection because nucleic acid would inherently be associated with NLS as recited in the instant claims.

Claims 13 and 40 have been included because Sutrave, Kuhn and Calos taught a method to produce transgenic chicken showing the expression of transgene in blood and egg white, therefore, it would inherently be also present in sperm of male offspring similar to one claimed in instant application

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Claims 1-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Macarthur et al (WO 97/47739, IDS), Tanaka et al (J Repord. Fert., 1994, Vol. 100, 447-449, IDS) and Calos (US 6,632672, dated 10/14/2003, IDS) or Kuhn et al (WO 02/38613, dated 5/16/2002; IDS) and Pollard et al (The Journal of Biological Chemistry 273, 13, 1998, 7507-7511, IDS).

The combined teachings of Calos/Kuhn have been discussed above and are relied in same manner here. However, none of the references explicitly teaches a method of producing transgenic avian by also introducing into avian cell a cationic polymer along with construct.

Macarthur et al teach a method for producing transgenic avian by transferring a transgene to an embryonic chicken cell, so as to create a transgenic hen wherein the transgene is expressed in the hen's oviduct and the transgene product is secreted in the hen's eggs and particularly egg white and/or those of her offspring (See abstract). Macarthur et al teach the vector comprises a portion of a retroviral genome, capable of transfecting a cell and incapable of replication comprising a transgene, operatively-linked to appropriate control elements such that the transgene may be expressed in a tissue specific manner (see page 3, lies 21-35). It is noted that Macarthur et al disclose a number of tissue specific promoter and signal sequence directing the uptake and secretion of the transgene product into the egg yolk (see page 3, lines 30-35). Macarthur et al also teach that the vectors may be used to introduce a nucleic acid sequence into germ cells and stem cells of an embryo of a chicken or it could be microinjected in a directly beneath the blastoderm of newly laid egg. The egg is then sealed and incubated until the chicken is hatched from the egg (see page 4, lines 12). Macarthur et al teach purified protein may be prepared for pharmaceutical use for several gene including one that encodes a blood clotting protein such as factor VIII, erythropoietin antibodies and immunoreactive portions thereof thus meets the limitations

of other fragments of an antibody and other proteins such as interferon as recited in the instant application (see page 5, lines 28 bridging to page 6 lines 1-7).

Macarthur et al also teach control elements that flank the transgene include promoters and enhancers, UTRs and signal sequence(s) that allow tissue specific expression of the transgene including several tissue specific promoters such as ovalbumin, lysozyme, conalbumin and ovomucoid promoters, and combinations thereof. It is noted that Macarthur et al also disclose signal sequences in the vector to direct secretion of the transgene product into the egg white and enhancers such as SV40 enhancer, or portion thereof (see page 6 lines 15-25). Macarthur et al exemplified a control elements which flank the gene of interest include the SV40 enhancer, three tandem estrogen response elements (ERE), 1.3 kb of the ovalbumin promoter (5' flank), 77 bp of 5' untranslated region (UTR), the N-terminal signal peptide sequence from the chicken lysozyme gene, and the polyadenylation and termination signals from the SV40 small T antigen comprising NLS (see Figure 2 and page 6 last paragraph). Macarthur et al teach methods to produce transgenic avians by microinjecting the vector is in a newly laid chicken egg arrested at stage X, in close proximity to, e.g., directly underneath, the blastoderm. After microinjection, the egg is sealed with shell membrane and a sealing material. The sealed egg is then incubated for various time up to and including the time of hatching to allow normal embryo growth and development. DNA from embryos and from newly hatched chicks is tested for the presence of sequences from the microinjected vector. It is also noted that Macarthur show the gene expression in the blood, sperm (see example 1) or eggs. Although, Macarthur et al embraced any method

to produce transgenic avian known in the art and also disclosed using lipofectamine for transfecting cell (see page 30, line 20), he did not explicitly teach the use of cationic polymer and that the embryos were introduced into an oviduct of a recipient hen.

However, Tanaka taught delivering DNA to an embryo, then delivering the embryo to the oviduct of a recipient hen (pg 449, col. 1, last paragraph). The embryo hatched and became a chick (pg 447, col. 2, "Materials and Methods;" pg 448, Fig. 1; pg 448, col. 1, line 4; pg 448, col. 2, 1st full paragraph, line 9). However, Tanak et al do not using NLS or cationic polymer in making transgenic avian.

Prior to instant invention, Pollard et al teach cationic polymer such as polyethyleneimine but not cationic lipid promoter the gene delivery from cytoplasm to nucleus and suggested that transgene expression is in fact prevented by complexation with cationic lipids but not with cationic polymer (see abstract, figure 2). However, Pollard et al do not teach a method of making transgenic avian

Accordingly, in view of the teachings of Macarthur, it would have been obvious for one of ordinary skill in the art, at the time the claimed invention was made, to modify the method of producing transgenic chicken taught by Macarthur to deliver virus encoding an exogenous protein under the control of the exogenous promoter into an embryo by microinjection and allow the embryo to become a chick as taught by Macarthur wherein the embryo was introduced into a recipient hen's oviduct as described by Tanaka. One of ordinary skill in the art at the time the invention was made would have been motivated to transplant the embryo of Macarthur into the oviduct of a recipient hen to provide the most natural environment for the embryo and to avoid

artificial methods of incubating the embryo. The skilled artisan would be further motivated to use a cationic polymer instead of a cationic lipid to enhance the gene expression in nucleus as taught by Pollard to microinject transgene with phiC31taught by Calos or nucleic acid encoding (phiC31 and NLS) fusion protein taught by Kuhn et al for making transgenic nonhuman animal with a reasonable expectation of success. One of ordinary skill in the art would have been sufficiently motivated to make such a modification, as Calos had described benefits of using alternative methods such as phiC31 or cre based recombinase for stable integration of transgene as compared to retroviral vector in producing transgenic nonhuman animal including chicken (supra). In addition, Calos/Kuhn sought to create transgenic nonhuman animal including chicken using recombinase based method for site-specific stable integration of transgene in the genome. Therefore, given that phiC31 based recombinase and NLS were available for use to integrate gene of interest in chicken as per the teachings of Calos/Kuhn, it would have obvious for an artisan to use the method of Macarthur and Tanaka to include phiC31 based recombinase with NLS and cationic polymer such as PEI to create transgenic chicken to produce human protein as disclosed in the instant application.

One who would practiced the invention would have had reasonable expectation of success because Macarthur and Tanaka had already described the method to produce transgenic chicken to produces any protein for pharmaceutical purpose, while Pollard had shown enhanced gene expression by using cationic polymer and not by cationic lipid. Calos/Kuhn had described use of other recombinase and NLS that could have been used in conjunction with the construct for making transgenic chicken to

express gene of interest. Thus, it would have only required routine experimentation to modify the method disclosed by Macarthus and Tanaks to include nucleic acid comprising integrase activity with NLS and cationic polymerto make transgenic chicken to produce human protein as required by instant invention.

Thus, Applicants' claimed invention, as a whole is *prima facie* obvious in the absence of evidence to the contrary.

Claims 9-10 and 36-37 have been included in the rejection because nucleic acid would inherently be associated with NLS as recited in the instant claims.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-55 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 53-80 and 92-101 of copending Application No. 10/790,455.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to methods of producing transgenic avians that uses serine recombinase mediated recombination at the heterologous recombination site mediated recombination at the heterologous recombination site. Since the specification of the '455 contemplated pHiC31 integrase mediated recombination between att site with in the nucleic acid molecule and an attachment site within the genomic DNA of avian cell and dependent embrace same production of same cytokines. Furthermore, instant application also discloses use of BAC to produce monoclonal antibody using the method essentially recited in application '455. Claim 1 of instant application is directed to a method of producing a transgenic avian by introducing into an avian cell a nucleic acid comprising a transgene, an integrase activity and a cationic polymer; introducing the avian cell into a recipient avian wherein the recipient avian produces an offspring which includes the transgene, thereby producing a transgenic avian. Subsequent claims 2-28 limit the method of claim 1to include specific stage of avian embryo and nuclear localization signal and transgene comprising coding sequence that is expressed as human antibody or cytokine. Claims are also directed to the transgenic avian and egg produced by the method of claim 1. Whereas claim 53-80 and 92-101 of application '455 application are directed to a

method of making a trisomic avian by isolating mitotic chromosome and then injecting the chromosome into an early stage embryo; and maintaining the embryo under conditions suitable for the embryo to develop and hatch as a chick. Subsequent claims limit the method to include heterologous recombination site is attP or coding sequence. It is noted that claims 92-101 are directed to a transgenic avian comprising a cell that contains an artificial chromosome subsequently limiting to a chicken comprising serine recombinase that mediates the recombination at the heterologous recombination site. Thus, the claims of application no 10/790,455 differs only with respect to broader scope of vector that could be used in the method for producing transgenic avians for producing desired polypeptide, which encompasses the nucleic acid comprising a transgene and integrase activity as claimed in instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-55 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-109 of copending Application No. 10/940,315.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to methods of producing transgenic chicken that uses serine recombinase mediated recombination at the heterologous recombination site mediated recombination at the heterologous recombination site to produce cytokine. Since the specification of the '315 contemplated serine recombinase

mediated recombination between att site with in the nucleic acid molecule and an attachment site within the genomic DNA of avian cell and dependent claims embrace production of protein (see paragraph . Claim 1 of instant application is directed to a method of producing a transgenic avian by introducing into an avian cell a nucleic acid comprising a transgene, an integrase activity and a cationic polymer; introducing the avian cell into a recipient avian wherein the recipient avian produces an offspring which includes the transgene, thereby producing a transgenic avian. Subsequent claims 2-28 limit the method of claim 1to include specific stage of avian embryo and nuclear localization signal and transgene comprising coding sequence that is expressed as human antibody or cytokine. Claims are also directed to the transgenic avian and egg produced by the method of claim 1. Whereas claim 1-101 of application '315 application are directed to a method of making a method of producing a transgenic vertebrate animal comprising: introducing into an embryo of a vertebrate animal a recombination site such that the recombination site is present in ovum of a mature vertebrate animal developed from the embryo. It is noted that subsequent claims limit the vertebrate animal to include a chicken comprising serine recombinase that mediates the recombination at the heterologous recombination site. Thus, the claims of application no 10/940,315 differ only with respect to broader scope of animal that could be used for producing desired polypeptide, which encompasses the nucleic acid comprising a transgene and integrase activity as claimed in instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-55 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-33 of copending Application No. 11/068,155.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to methods of producing transgenic avians that uses serine recombinase mediated recombination at the heterologous recombination site mediated recombination at the heterologous recombination site to produce polypeptide or antibodies. Since the specification of the '155 contemplated serine recombinase mediated recombination between att site with in the nucleic acid molecule and an attachment site within the genomic DNA of avian cell and dependent embrace same production of same cytokines (see paragraph 31 and 49 of the specification). Claim 1 of instant application is directed to a method of producing a transgenic avian by introducing into an avian cell a nucleic acid comprising a transgene, an integrase activity and a cationic polymer; introducing the avian cell into a recipient avian wherein the recipient avian produces an offspring which includes the transgene, thereby producing a transgenic avian. Subsequent claims 2-28 limit the method of claim 1to include specific stage of avian embryo and nuclear localization signal and transgene comprising coding sequence that is expressed as human antibody or cytokine. Claims are also directed to the transgenic avian and egg produced by the method of claim 1, whereas claim 1-33 of application '155 are directed to a method of producing a transchromosomic avian. It is noted that subsequent claims limit the avian to include a chicken, quail or turkey. It is also noted that specification contemplate using serine

recombinase that mediates the recombination at the heterologous recombination site. Thus, the claims of application no 11/068155 differ only with respect to broader scope of vectors that could be used for producing transgenic avians for producing desired polypeptide, which encompasses the nucleic acid comprising a transgene and integrase activity as claimed in instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-55 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-28 of copending Application No. 11/193,750.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to methods of producing transgenic avians that uses serine recombinase mediated recombination at the heterologous recombination site mediated recombination at the heterologous recombination site to produce polypeptide or antibodies. Since the specification of the '750 contemplated serine recombinase mediated recombination between att site with in the nucleic acid molecule and an attachment site within the genomic DNA of avian cell and dependent embrace same production of same cytokines (see paragraph 27, 29, 31 and 49 of the specification). Claim 1 of instant application is directed to a method of producing a transgenic avian by introducing into an avian cell a nucleic acid comprising a transgene, an integrase activity and a cationic polymer; introducing the avian cell into a recipient avian wherein the recipient avian produces an offspring which includes the transgene,

thereby producing a transgenic avian. Subsequent claims 2-28 limit the method of claim 1to include specific stage of avian embryo and nuclear localization signal and transgene comprising coding sequence that is expressed as human antibody or cytokine. Claims are also directed to the transgenic avian and egg produced by the method of claim 1, whereas claim 1-28 of application '750 are directed to a method of producing a transchromosomic avian. It is noted that subsequent claims limit the avian to include a chicken, quail or turkey. It is also noted that specification contemplate using serine recombinase that mediates the recombination at the heterologous recombination site. Thus, the claims of application no 11/193,750 differ only with respect to broader scope of vectors that could be used for producing transgenic avians for producing desired polypeptide, which encompasses the nucleic acid comprising a transgene and integrase activity as claimed in instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Hadlaczky et al (US 6,743,967)

Harvey et al (WO/56932).

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anoop Singh whose telephone number is (571) 272-3306. The examiner can normally be reached on 9:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272- 0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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